

### **REMARKS/ARGUMENTS**

Prior to the present amendment, Claims 58-77 were pending in this application. With this amendment, Claim 66-67 and 71-73 have been cancelled without prejudice, and Claims 58-65 and 68-70 have been amended, and new Claims 78-84 have been added. Claims 58-65, 68-70 and 74-84 are pending after entry of the instant amendment. Applicants expressly reserve the right to pursue any canceled matter in subsequent continuation, divisional or continuation-in-part applications.

The specification has been amended to correct formal errors as discussed below. Claims 58-65 and 68-69 have been amended to clarify what applicants have always regarded as their invention. The amendments to the specification and claims are fully supported by the specification and claims as originally filed and do not constitute new matter. New Claims 78-84 are fully supported by the specification and the claims as originally filed. Support for new Claims 78-84 can be found in the specification at least, for example, on page 107, lines 30-34 and on page 129, lines 27-36.

#### **Specification**

The title was objected to as being non-descriptive. The foregoing amendment, which replaces the original title with a new, descriptive title is believed to overcome this objection.

As requested by the Examiner, Applicants have amended the specification to correct the ATCC address on page 376, line 34. The foregoing amendment is believed to overcome this objection.

In addition, the specification has been amended to remove embedded hyperlink and/or other form of browser-executable code.

Applicants would like to indicate that Applicants recently made a photocopy of U.S. Application 09/918,585 filed 7/30/2001, of which the instant application is a continuation, from the PTO's files. Applicants respectfully submit that all references to page and line numbers made throughout this response will be based on the application photocopied from the PTO files by the Applicants.

### **Information Disclosure Statement**

The Examiner notes that references cited as "BLAST Results", filed on April 30, 2002, do not give sufficient identifying information. In response, Applicants file herewith, an Information Disclosure Statement listing each reference of the "Blast Search" separately and including authors/inventors, relevant accession numbers and publication dates. Applicants respectfully request that the listed information be considered by the Examiner and be made of record in the above-identified application.

### **Priority Determination**

Applicants rely on the gene amplification assay (Example 114) for support of patentable utility. This data was first disclosed in U.S. Provisional Application 60/113,296 filed on December 22, 1998, the priority of which is claimed in the present application.

### **Claim Rejections – 35 U.S.C. §112, Second Paragraph**

Claims 58-77 are rejected under 35 U.S.C. §112, second paragraph, for allegedly "being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." The Examiner notes that "[c]laims that recite 'the extracellular domain' of the protein are indefinite as no extracellular domain has been described. Therefore, the metes and bounds of the claims cannot be determined. For example see Claims 58-63, parts (c) and (d)." Further, the Examiner alleges that "if the protein had an extracellular domain, the recitation of 'the extracellular domain' ... 'lacking its associated signal sequence' (Claim 58, part (d), for example) is indefinite[.]"

Without acquiescing to any of the rejections, Applicants submit that the cancellation of Claims 66, 67 and 71-73 renders the rejection of these claims moot. Furthermore, the terms "extracellular domain" and "extracellular domain ... lacking its associated signal peptide" are no longer present in Claims 58-63. Accordingly, Applicants request that the rejection of Claims 58-65, 68-70 and 74-77 under 35 U.S.C. §112, second paragraph, be withdrawn.

Claims 71 and 72 are further rejected under 35 U.S.C. § 112, second paragraph, because the terms "hybridizes to" and "stringent conditions" are indefinite.

Without acquiescing to these rejections, Applicants submit that the cancellation of

Claims 71-73 renders the rejection of these claims moot. Accordingly, Applicants request that the rejection of Claims 71 and 72 under 35 U.S.C. §112, second paragraph, be withdrawn.

**Claim Rejections – 35 U.S.C. §112, First Paragraph (Enablement)**

Claims 58-62 and 71-77 are rejected under 35 U.S.C. §112, first paragraph, allegedly because "the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims." The Examiner further notes that "the specification, while being enabling for the nucleic acid of SEQ ID NO: 205 or fragments of such that re usable as hybridization probes, does not reasonably provide enablement for nucleic acids 80, 85, 90, 95 or 99% identical to such, nor which encode a protein 80, 85, 90, 95 or 99% identical to the protein of SEQ ID NO:205, nor nucleic acids which hybridizes to any of the above." Applicants respectfully disagree.

Applicants submit that the cancellation of Claims 71-73 renders the rejection of these claims moot.

With respect to Claims 58-62 and 74-77, without acquiescing to the rejection, Applicants respectfully submit that amended Claims 58-62, and 74-77 now recite a credible, specific and substantial utility, by reciting the requirement that the nucleic acid is amplified in lung or colon tumors. Support for this recitation is found at least in Example 114.

Example 114 of the present application describes in detail the isolation of genomic DNA from a variety of primary cancers and cancer cell lines that are listed in Table 8, including primary lung cancers of the type and stage indicated in Table 8. As a negative control, DNA was isolated from the cells of ten normal healthy individuals, which was pooled and used as a control. Gene amplification was monitored using real-time quantitative TaqMan PCR. Table 9 shows the resulting gene amplification data. Further, Example 114 explains that the results of TaqMan™ PCR are reported in  $\Delta C_t$  units, wherein one unit corresponds to one PCR cycle or approximately a 2-fold amplification relative to control, two units correspond to 4-fold amplification, 3 units to 8-fold amplification etc. PRO853 showed approximately 1.03-1.33  $\Delta C_t$  units which corresponds to  $2^{1.03}$ - $2^{1.33}$ - fold amplification or 2.042 fold to 2.514-fold amplification in lung tumors. PRO853 also showed approximately 1.11-2.4  $\Delta C_t$  units which corresponds to  $2^{1.11}$ - $2^{2.4}$ - fold amplification or 2.158 fold to 5.278-fold amplification in colon tumors.

Applicants respectfully submit that based on the teachings of Example 114, the general knowledge available in the art at the priority date of the invention, and the high percentage of sequence identity recited in the rejected claims, one skilled in the art would be able to practice the claimed invention in its full scope without any undue experimentation. As the M.P.E.P. states, "The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation" *In re Certain Limited-charge cell Culture Microcarriers*, 221 USPQ 1165, 1174 (Int'l Trade Comm'n 1983), *aff. sub nom.*, *Massachusetts Institute of Technology v A.B. Fortia*, 774 F.2d 1104, 227 USPQ 428 (Fed. Cir. 1985) M.P.E.P. 2164.01.

Furthermore, based on the instant disclosure, which details how to make and use nucleic acid variants and the advanced knowledge in the art at the time of filing, one skilled in the art would know exactly how to make and use these nucleic acids for the diagnosis of lung and colon tumors; for example, by using diagnostic methods based on hybridization to such amplified sequences.

Accordingly, Applicants respectfully request the Examiner to reconsider and withdraw the rejection of Claims 58-62 and 74-77 under 35 U.S.C. § 112, first paragraph.

**Claim Rejections – 35 U.S.C. §112, First Paragraph (Written Description)**

Claims 58-62 and 71-77 are rejected under 35 U.S.C. §112, first paragraph, for alleged lack of sufficient written description. The Examiner asserts that claims drawn to polynucleotides having at least 80%, 85%, 90%, 95% or 99% sequence identity with the claimed sequence do not recite that it encodes a particular protein or any biological activity or any conserved structure or any distinguishing feature. Thus, the Examiner notes that in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Applicants submit that the cancellation of Claims 71-73 renders the rejection of these claims moot.

With respect to Claims 58-62 and 74-77, without acquiescing to the rejection, Applicants respectfully submit that amended Claims 58-62, and 74-77 now recite a credible, specific and substantial utility, by reciting the requirement that the nucleic acid is amplified in lung or colon

tumors. Support for this recitation is found at least in Example 114. This biological activity, coupled with a well defined, and relatively high degree of sequence identity is believed to sufficiently define the claimed genus, such that one skilled in the art would readily recognize that the Applicants were in the possession of the invention claimed at the effective filing date of this application. Hence, the present rejection should be withdrawn.

#### **Deposit Requirement**

Claims 58-63 and 70-77 are rejected under 35 U.S.C. §112, first paragraph, allegedly for "containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims."

Applicants submit that the cancellation of Claims 71-73 renders the rejection of these claims moot.

With respect to Claims 58-63 and 74-77, without acquiescing to the Examiner's rejection, the sentence beginning on page 378, line 35 has been amended to state, "This assures maintenance of a viable culture of the deposit for 30 years from the date of deposit and for at least five (5) years after the most recent request for furnishing of a sample of the deposit."

Accordingly, Applicants believe that all of the requirements of 37 C.F.R. § 1.806 are met and the Examiner is respectfully requested to reconsider and withdraw the rejection of Claims 58-63 and 74-77 under 35 U.S.C. §112, first paragraph.

#### **Claim Rejections – 35 U.S.C. §102**

Claims 71-73 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Matsubara *et al.*, WO 95/14772. Applicants respectfully submit that the cancellation of Claims 71-73 renders the rejection of these claims moot.

The present application is believed to be in *prima facie* condition for allowance, and an early action to that effect is respectfully solicited. Should there be any further issues outstanding, the Examiner is invited to contact the undersigned attorney at the telephone number shown below.

Please charge any additional fees, including fees for additional extension of time, or credit overpayment to Deposit Account No. 08-1641 (referencing Attorney's Docket No. 39780-2630 P1C73).

Respectfully submitted,

Date: July 20, 2004

By:   
Anna L. Barry (Reg. No. 51,436)

**HELLER EHRMAN WHITE & McAULIFFE LLP**  
275 Middlefield Road  
Menlo Park, California 94025  
Telephone: (650) 324-7000  
Facsimile: (650) 324-0638

SV 2022092 v1  
7/20/04 9:21 AM (39780.2630)